PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 6 : A61L 29/00, 31/00, 27/00

A1

(11) International Publication Number: WO 99/32168

(43) International Publication Date: 1 July 1999 (01.07.99)

(21) International Application Number: PCT/US98/27202

(22) International Filing Date: 21 December 1998 (21.12.98)

(30) Priority Data:
08/996,022 22 December 1997 (22.12.97) US

(71) Applicant: BECTON DICKINSON AND COMPANY [US/US]; One Becton Drive, Franklin Lakes, NJ 07417-1880 (US).

(72) Inventors: KHAN, Mohammad, A.; 10005 South Falcon Hurst Drive, Sandy, UT 84092 (US). ORR, Douglas, P.; 9214 Stone View Cove, Sandy, UT 84093 (US).

(74) Agent: LEE, Eric, M.; Becton Dickinson and Company, One Becton Drive, Franklin Lakes, NJ 07417-1880 (US).

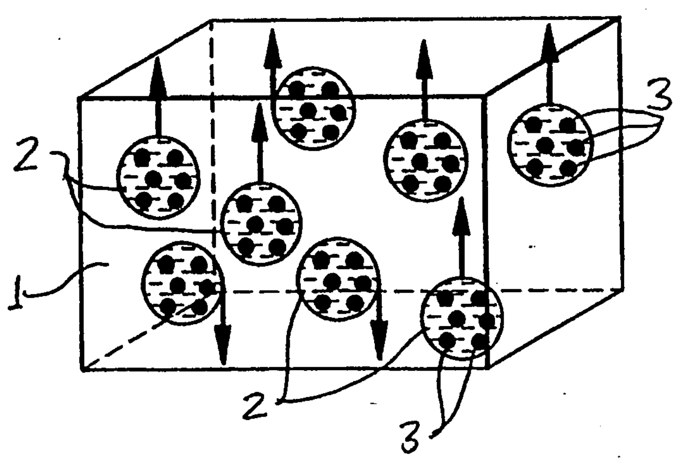
(81) Designated States: AU, BR, CA, CN, JP, MX, SG, European patent (AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE).

Published
With international search report.

(54) Title: A MATERIAL FOR USE IN MEDICAL DEVICES WITH A SELF-REPLENISHING ANTIMICROBIAL AND/OR LUBRICIOUS SURFACE

(57) Abstract

The material of this invention provides a continual supply of an antimicrobial agent and/or a lubricious agent to the surface thereof. A carrier may be used to facilitate the migration of the antimicrobial and/or lubricious agents to the surface of the material. These agents migrate to the surface as a result of the incompatibility, i.e. low miscibility and low solubility of the antimicrobial and/or lubricious agents and carrier, it one is used, with the base material that is used to form the medical device. In a preferred embodiment, the base material (1) is a silicone elastomer, the carrier (2) is siloxane oil and thus also acts as the lubricating agent oil and the antimicrobial agent (3) is chlorhexidine.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AL	Albania	ES	Spain	LS	Lesotho	SI	Slovenia
AM	Armenia	FI	Finland	LT	Lithuania	SK	Slovakia
AT	Austria	FR	France	LU	Luxembourg	SN	Senegal
AU	Australia	GA	Gabon	LV	Latvia	SZ	Swaziland
AZ	Azerbaijan	GB	United Kingdom	MC	Monaco	TD	Chad
BA	Bosnia and Herzegovina	GE	Georgia	MD	Republic of Moldova	TG	Togo
BB	Barbados	GH	Ghana	MG	Madagascar	TJ	Tajikistan
BE	Belgium	GN	Guinea	MK	The former Yugoslav Republic of Macedonia	TM	Turkmenistan
BF	Burkina Faso	GR	Greece			TR	Turkey
BG	Bulgaria	HU	Hungary	ML	Mali	TT	Trinidad and Tobago
BJ	Benin	IE	Ireland	MN	Mongolia	UA	Ukraine
BR	Brazil	IL	Israel	MR	Mauritania	UG	Uganda
BY	Belarus	IS	Iceland	MW	Malawi	US	United States of America
CA	Canada	IT	Italy	MX	Mexico	UZ	Uzbekistan
CF	Central African Republic	JP	Japan	NE	Niger	VN	Viet Nam
CG	Congo	KE	Kenya	NL	Netherlands	YU	Yugoslavia
CH	Switzerland	KG	Kyrgyzstan	NO	Norway	ZW	Zimbabwe
CI	Côte d'Ivoire	KP	Democratic People's Republic of Korea	NZ	New Zealand		
CM	Cameroon			PL	Poland		
CN	China	KR	Republic of Korea	PT	Portugal		
CU	Cuba	KZ	Kazakstan	RO	Romania		
CZ	Czech Republic	LC	Saint Lucia	RU	Russian Federation		
DE	Germany	LI	Liechtenstein	SD	Sudan		
DK	Denmark	LK	Sri Lanka	SE	Sweden		
EE	Estonia	LR	Liberia	SG	Singapore		

A MATERIAL FOR USE IN MEDICAL DEVICES WITH A SELF-REPLENISHING ANTIMICROBIAL AND/OR LUBRICIOUS SURFACE

Background of the Invention

This invention relates to materials for use with medical devices. More particularly, this invention relates to materials that exhibit antimicrobial activity and lubricity at the surface of the material. Even more particularly, this invention relates to materials where the antimicrobial activity and lubricity present at the surface of the material is maintained over a period of time.

Various materials are used to fabricate medical devices and other apparatuses used in medical diagnosis or treatment. Frequently, polymeric materials are used for such devices because of their stability and biocompatibility. Such polymeric materials include polytetrafluoroethylene, polyurethane, polyethylene and silicone. A typical application for these polymeric materials is to form various types of catheters that are used to infuse fluid, such as medicaments and nutrition, into a patient, to withdraw fluid from a patient, or to provide access to an internal site in a patient to perform a diagnositic or treatment procedure on the patient. Another application for these polymeric materials is to form injection sites, valves and medical tubing and other related devices used in infusion therapy. Since all of these products are used in close proximity to a patient, and in some cases are inserted into the patient's body, or include moving parts, infection control and lubricity are important issues that must be addressed.

Infection control is an especially acute problem for certain types of medical devices that come into contact with body fluids or tissues through an opening in the skin. Where an incision or puncture is made in a patient's skin to provide a path for the medical device to reach the patient's vasculature or other internal location, such an incision or puncture provides a direct path for microorganisms to enter and infect the body. Typically, such microorganisms colonize the area near the device where body fluids may pool and then these microorganisms migrate along the medical device into the patient's body and cause infection. Such an infection is unpleasant for the patient and must be treated. Such treatment results in increased expense to the health care facility. In certain circumstances such an infection can be life threatening for the patient. As a result, the clinician using the medical device must maintain the area where the incision or puncture is to be made in the patient's skin as sterile as possible.

Preferably this area should be devoid of any live microorganisms to prevent these microorganisms from reaching the patient and causing an infection.

Various protocols are used to maintain such a sterile field and to minimize the chances for infection to reach the patient. In many instances, an antimicrobial agent such as iodine, is wiped with a cotton gauze material over the patient's skin at the area where the incision or puncture is to be made to kill any microorganisms that may be alive on the patient's skin. Thus when the medical device is inserted through the skin the chances of any microorganisms being transferred into the patient's body with the medical device is minimized. In addition, various portions of the medical device in proximity to this area may also be wiped with an antimicrobial agent to minimize the chances for infection to occur. This is especially so in cases where a valve is located at the proximal end of a catheter that allows intermittent injection of fluid into the patient through the catheter. Prior to insertion of a device into the valve, the valve is swabbed with an antimicrobial agent to minimize the chances that any microorganisms located on the valve will be injected into the patient with the fluid.

Lubriciousness is an important issue for the patient in those cases where the medical device is to be inserted into the patient's body. Where the outer surface of the medical device is lubricious, any pain felt by the patient as the device is being inserted into the patient is minimized. This is because there is a minimal amount of drag between the patient's skin and the medical device. In addition, in those medical devices where there are moving parts, such as in valves, lubriciousness of the moving parts ensures that the device will work through repeated cycles of use without the device binding or otherwise failing due to excessive friction between the moving parts.

In an effort to deal with the problems of infection control and lubriciousness of medical devices, an antimicrobial agent, i.e. any agent which acts to inhibit the growth of microorganisms, such as pathogenic bacteria, protists and fungi, which can cause infections in a patient, and a lubricating agent can be applied to the surface of the medical device. Although this solution to the problem may be acceptable in certain situations, it is not universally acceptable. One shortcoming of merely applying the antimicrobial agent and the lubricating agent to the surface of the medical device is that these agents may be inadvertently wiped from the medical device during handling. Thus the effects of these agents may be entirely eliminated from the medical device prior to the device ever being applied to or inserted into the patient.

Instead of merely applying the antimicrobial agent and the lubricating agent to the surface of the medical device, these agents may be blended into, compounded with or otherwise embedded into the polymeric materials that are used to form the medical

device. This compounding purportedly changes the surface characteristics of the material or allows dissolution of the agents from the material into the surrounding environment. Alternatively, in appropriate circumstances the medical device may be formed by coextruding a base layer of the polymeric material with an outer layer of another material that is antimicrobial and lubricious. This outer layer thus provides the anti-infective and lubricious characteristics desired for the medical device. Unfortunately, both of these mechanisms are expensive because they add another processing step to the manufacturing process. In addition, the coextrusion process is impractical for certain medical devices that are formed by injection molding and that can not be manufactured by coextrusion.

Summary of the Invention

It is therefore an object of this invention to provide a material that exhibits an antimicrobial effect at the surface thereof and that is especially adapted for use in producing medical devices.

It is another object of this invention to provide a material that exhibits an antimicrobial effect at the surface thereof and that has a lubricious surface and that is especially adapted for use in producing medical devices.

It is yet another object of this invention to provide a material that exhibits an antimicrobial effect at the surface thereof and that has a lubricious surface and where those characteristics are continually replenished even if the surface of the material is wiped or otherwise used in the normal course of medical procedures.

It is a further object of this invention to provide a material that has an antimicrobial effect at the surface thereof and that has a lubricious surface and that is relatively simple and inexpensive to manufacture.

In one embodiment of this invention, the base material that is used for producing the medical device incorporates an antimicrobial agent that can migrate to the surface of the base material. In another embodiment of this invention, the base material incorporates a lubricating agent that can migrate to the surface of the base material. In another embodiment of this invention, the base material incorporates both an antimicrobial agent and a lubricating agent that both can migrate to the surface of the base material. In each of these embodiments, the antimicrobial agent and/or the lubricating agent may be mixed with a carrier or may be dispersed in the base material alone. The carrier facilitates the migration of the antimicrobial agent and/or the lubricating agent to the surface of the base material. In a preferred embodiment, the carrier can act as both a lubricating agent and a carrier for the antimicrobial agent.

Where a carrier is used, the carrier must not adversely affect the antimicrobial and lubricating characteristics of the agents mixed therein. In addition, the antimicrobial and/or lubricating agents must be compatible with the carrier. This means that these materials must be miscible or dispersible and have solubility with respect to one another. In addition, the carrier on the one hand and the antimicrobial agent and the lubricating agent on the other hand, if no carrier is used, must not be compatible with the base material that is used to form the medical device. This means only that the materials are not miscible and have a low solubility with respect to one another. This incompatibility ensures that the carrier or the antimicrobial and/or lubricating agents, if no carrier is used, migrates to the surface of the base material. This incompatibility can be achieved by having one material hydrophobic and the other material hydrophilic. And since the carrier does not affect the antimicrobial and/or lubricating effects of the agents mixed therein, when the carrier migrates to the surface it provides a film on the surface of the base material that has antimicrobial activity and/or that is lubricious.

The migration of the carrier, with the antimicrobial agent and/or the lubricating agent, to the surface of the base material continues as long as a certain minimum amount of the carrier remains in the base material. Thus if the medical device formed from the base material is wiped with a solvent such as isopropyl alcohol, which is a typical topical disinfectant used in health care settings, the surface of the medical device is cleaned of any dead microorganisms. In addition, the carrier continues to migrate to the surface so the antimicrobial agent and/or the lubricating agent continue to be available at the surface of the medical device. As a result, the surface of the medical device formed from the material of this invention continues to have an antimicrobial effect and/or that continues to be lubricious for a long period of time.

The antimicrobial agent and/or the lubricating agent alone can be blended with or compounded into the base material. Alternatively where a carrier is used, the antimicrobial agent and/or the lubricating agent are mixed with the carrier which is then blended with or compounded into the base material. Thereafter, the base material is formed into the desired medical device by standard extrusion or injection molding operations.

Brief Description of the Drawings

The preferred embodiments are illustrated in the drawings in which like reference numerals refer to like elements and in which:

FIG. 1 is a graphic representation of a block of base material with the antimicrobial agent encapsulated in a lubricious carrier which is located in the matrix of the base material; and

FIG. 2 is a graphic representation of a block of base material with the antimicrobial agent and the lubricious carrier forming a film on the surface of the block of base material after some of the carrier has migrated to the surface to form a film on the surface of the block of base material.

Detailed Description of the Invention

The material of this invention provides a continual supply of antimicrobial and/or lubricious agents to the surface of the base material as long as a certain minimum amount of those agents remains in the base material. A carrier can be used if desired to facilitate the migration of these agents to the surface of the base material. Where a carrier is used, the carrier must be compatible with the antimicrobial and/or lubricious agents and must not affect the antimicrobial and/or lubricious nature of those agents. The term compatible as used herein means that the materials are miscible or dispersible, i.e. mix well, with one another, and have solubility, i.e. the solute will not precipitate out of solution, with respect to each other. However, in order for this migration to occur, the carrier must be incompatible with the base material that is used to form the medical device. As used herein the term incompatible means that the two materials are not miscible and have a low solubility with respect to one another. If no carrier is used, then the antimicrobial and/or lubricating agents must be incompatible with the base material to ensure migration of these materials to the surface of the base material.

This incompatibility discussed above can be achieved where one material is hydrophobic and the other material is hydrophilic. As used herein, the term hydrophobic when used to describe a material means that the material is more hydrophobic as compared to the compared material. Similarly, the term hydrophilic when used to describe a material means that the material is more hydrophilic as compared to the compared material.

Typically in medical applications such as catheters and related infusion therapy devices, a polymeric material is used to form the medical device. Any polymeric material may be used for the base material however polymers such as polytetrafluoroethylene, polyurethane, polyethylene and silicone are preferably used because of their known biocompatibility and stability. These polymers are considered

to be hydrophobic. Thus, the base material of this invention will be described herein as being preferably hydrophobic.

The selection of the antimicrobial agent, the lubricating agent, and the carrier is ultimately dependent upon the base material that is used. As noted above, the base material tends to be hydrophobic so these materials must be hydrophilic, i.e. less hydrophobic than the base material.

The antimicrobial agent that is used in this invention should have a known and effective antimicrobial activity. Where no carrier is used with the antimicrobial agent, the antimicrobial agent must be incompatible with the base material. Where a carrier is used, the antimicrobial agent must be compatible with the carrier. In both cases the antimicrobial agent must not lose its antimicrobial activity while located in the matrix of the base material. Most antimicrobial agents are relatively hydrophilic and thus could be used alone in combination with one of the polymers identified above to achieve the benefits of this invention. Preferably, the antimicrobial agent used should be chlorhexidine, or one of its salts depending upon its solubility and miscibility with the chosen base material and carrier, if a carrier is used. Other antimicrobial agents such as iodine, other bis-biguanides, tricylosan, para-chloro-meta-xylenol can be used depending upon their miscibility and solubility with respect to the other material in the system.

The lubricating agent that is used in this invention should have a known and effective lubricating effect. Where no carrier is used, the lubricating agent, and where applicable the antimicrobial agent, must be incompatible with the base material. Where a carrier is used, the lubricating agent must be compatible with the carrier. In either case, the lubricating agent must not lose its lubricating effect while located in the matrix of the base material. Preferably a siloxane oil can be used as the lubricating agent.

Various carriers can be used in combination with the base material. In determining the appropriate carrier to use with a particular base material, two important factors must be considered. First, the carrier must not adversely affect the antimicrobial activity of the antimicrobial agent nor should it adversely effect the lubricating properties of the lubricating agent if one is used. Second, the carrier must be incompatible with the base material so that the carrier will not mix well or dissolve in the base material but will want to migrate out of the base material. The carrier can serve two functions at once if the carrier is an inherently lubricious material. In such a case, the carrier is the carrier for the antimicrobial agent and is the lubricating agent as well. For example, where the base material is a silicone elastomer, a fluorinated, phenylated, or diphenylated siloxane oil should be used as the carrier. This is because

the siloxane oil is incompatible with the silicone elastomer and has a tendency to come out of solution where the two are mixed together. In addition, the siloxane oil is inherently lubricious and does not have a deleterious effect on the antimicrobial agent.

Finally, the amount of each of the agents as well as the amount of the carrier that should be used with the base material is dependent upon the amount of antimicrobial and lubricating effect that is desired as well as the time period over which these agents are desired to provide the desired characteristics. In addition, another consideration to determining how much of the various materials that should be used in the system is the rate of diffusion of one material through another material. This is controlled by Fick's law of diffusion and depends on the molecular structure and packing of the polymer molecules. The diffusion rate also depends on the relative hydrophobicity and hydrophilicity of the various materials used in the system.

Where an antimicrobial agent is used in combination with a lubricious carrier, preferably the antimicrobial agent comprises between about 0.5% by weight and about 10% by weight of the carrier solution and the carrier solution comprises between about 1% by weight and about 10% by weight of the base material. Where only an antimicrobial agent is used, preferably the antimicrobial agent comprises between about 0.1% by weight and about 10% by weight of the base material. Where only a lubricating agent is used, preferably the lubricating agent comprises between about 1% by weight and about 10% by weight of the base material.

As shown in the FIGS., a block of base material 1 includes a carrier 2 that is dispersed in base material 1. Carrier 2 is lubricious and contains an antimicrobial agent 3 therein. In FIG. 1, carrier 2 is still located in the matrix of base material 1. In FIG. 2, both carrier 2 and antimicrobial agent 3 have migrated to the surface of base material 1 to provide the surface of base material 1 with an antimicrobial and lubricating effect. In a preferred embodiment, base material 1 is a silicone elastomer, carrier 2 is siloxane oil which acts as both a carrier and a lubricating agent and antimicrobial agent 3 is chlorhexidine. Various examples of the characteristics of this combination are provided below.

Example 1

In order to determine whether the carrier material would have an adverse effect on the antimicrobial activity of the antimicrobial agent, 6 millimeter diameter discs were cut from Whatman filter paper and a known amount of a solution comprised of 5% by weight of chlorhexidine in FS-300 fluorosilicone fluid was placed on the discs. Thereafter, the discs were placed on the surface of an agar plate which had been

previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The plate was incubated overnight and the resulting zone of inhibition around the disc was 18.2 millimeters for the S. aureus and 12.3 millimeters for the P. aeruginosa. This experiment showed that the fluorosilicone fluid carrier has no appreciable deleterious effect on the antimicrobial activity of the chlorhexidine.

Example 2

The following experiment was performed in order to determine whether the carrier material with the antimicrobial agent would migrate to the surface of the base material. A solution comprised of 5% by weight of chlorhexidine in FS-300 fluorosilicone fluid was prepared. 4% by weight of this solution was mixed with a liquid silicone rubber material having a durometer of 70A. The resulting mixture was cured and 8 millimeter squares having a thickness of 2 millimeters were formed. Thereafter, the squares were placed on the surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The resulting zone of inhibition three days after the manufacture of the squares was about 1 to 2 millimeters around the squares with no growth under the samples for both organisms.

As a control, the fluorosilicone fluid without the chlorhexidine was mixed with the liquid silicone rubber material. When the resulting squares were placed in the agar dish, no zone of inhibition was observed.

This experiment shows that the carrier with the antimicrobial agent migrates to the surface of the base material. At the surface, the antimicrobial agent still possesses antimicrobial effect.

Example 3

The following experiment was performed to determine whether the use of a different carrier would affect the antimicrobial activity of the antimicrobial agent. A solution containing 10% by weight of chlorhexidine diacetate in Carbowax 400 polyethylene glycol was formed. 4% by weight of this solution was then mixed with the liquid silicone rubber and 3 millimeter squares with a thickness of 4 millimeters were formed. Thereafter, the squares were placed on the surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The zone of inhibition for the S. aureus was 2 millimeters and for the P. aeruginosa no zone of inhibition was observed but there was no growth under the squares. When another sample was made using a solution containing 10% by

weight of chlorhexidine diacetate, 4% by weight of the liquid silicone rubber and the Carbowax 400 polyethylene glycol, the result was similar. The zone of inhibition for the S. aureus was 1 - 3 millimeters but there was no zone of inhibition for the P. aeruginosa but there was no growth under the squares.

Example 4

Various concentrations of chlorhexidine were tested with the fluorosilicone fluid. All of the resulting solutions were mixed with the liquid silicone rubber so that the solution comprised 4% by weight of the mixture. Discs were formed having a diameter of 6 millimeters and a thickness of between 1 millimeter and 2 millimeters. Thereafter, the discs were placed on the surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The results are tabulated below:

Sample Number	Chlorhexidine Concentration	Zone of Inhibition
1	2.91%	S.A. 9.7 mm P.A. 6.8 mm
2	4.76%	S.A. 11.7 mm P.A. 7.7 mm
3	7.41%	S.A. 13.7 mm P.A. 11 mm
4	4.76%	S.A. 15 mm P.A. 11 mm

In Sample Number 4, the carrier was a mixture of F-68 (1% by weight) and FS-300. The above example shows that this invention works at very low chlorhexidine concentrations.

Example 5

Various concentrations of chlorhexidine were tested with MPQ fluorosilicone oil. All of the resulting solutions were mixed with the liquid silicone rubber so that the solution comprised 4% by weight of the mixture. In samples 1 - 3 the liquid silicone rubber had a durometer of 70A, while in samples 4 - 6 the liquid silicone rubber was 7-6860. Discs were formed having a diameter of 6 millimeters and a thickness of between 1 millimeter and 2 millimeters. Thereafter, the discs were placed on the

surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The results are tabulated below:

Sample Number	Chlorhexidine Concentration	Zone of Inhibition
1	2.91%	S.A. 8.3 mm P.A. vague zone with no growth under sample.
2	4.76%	S.A. 8.3 mm P.A. vague zone with no growth under sample.
3	7.41%	S.A. 11 mm P.A. vague zone with no growth under sample.
4	2.91%	S.A. 9.3 mm P.A. vague zone with no growth under sample.
5	4.76%	S.A. 12.3 mm P.A. vague zone with no growth under sample.
6	7.41%	S.A. 10.3 mm P.A. vague zone with no growth under sample.

This experiment shows that MPQ is not as good a carrier for the antimicrobial agent as the fluorosilicone fluid when liquid silicone rubber is the base material.

Example 6

The following experiment was conducted to compare two different base materials. In the both samples a solution of 4.76% by weight of chlorhexidine and MPQ fluorosilicone oil as the carrier was prepared. In the first sample, 4% by weight of this solution was mixed with 7-6860 as the base material while in the second sample, 4% by weight of the solution was mixed with liquid silicone rubber having a durometer of 65A where the liquid silicone rubber contained 5% by weight of fluorosilicone fluid. In both samples discs having a diameter of 6 millimeters and a thickness of 1.5 millimeters

were formed. Thereafter, the discs were placed on the surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. The first sample had 13.7 millimeter zone of inhibition for S. aureus and a 1 millimeter zone of inhibition around the disc and no growth under the disc for P. aeruginosa. The second sample had a 11 millimeter zone of inhibition for S. aureus and no zone of inhibition but no growth under the disc for P. aeruginosa.

Example 7

The following experiment was conducted to determine if the salutory effects of this invention would appear with other base materials. In all of the samples, a solution comprising 4% by weight of chlorhexidine was mixed in the MPQ fluorosilicone oil carrier. The base material was either liquid silicone rubber having a durometer of 65A or HCRA silicone gum rubber having a durometer of 65A. The concentration of the solution in the base material was varied between 3% by weight and 5% by weight. Discs having a diameter of 5 millimeters and a thickness of 1.5 millimeters were formed. Thereafter, the discs were placed on the surface of an agar plate which had been previously swabbed for confluent growth using a broth suspension of either S. aureus or P. aeruginosa. In all of the samples both organisms responded similarly and the zones of inhibition were comparable, viz. on day 1 there was a 1 mm zone of inhibition but on subsequent days there was no zone of inhibition but no growth under the samples.

Example 8

Needleless access valve devices such as disclosed in U.S. Patent Application Serial No. 08/345,481, now U.S. Patent No. (P-3885P2) were tested with this invention. Such a needleless access valve device uses a movable plug that moves in the housing of the device to open and close the device to fluid flow. The movable plugs in this example were formed from HCRA silicone gum rubber. In the test, a series of devices was made where the movable plug did not have a lubricant dispersed in the base material of the plug. Another series of devices was made where the movable plug included 4% by weight of an FS 300 fluorosilicone oil lubricant dispersed in the base material of the plug. The actuation force needed to open the needleless access valve by moving the movable plug past the opening to the fluid flow channel was noted for the devices. Where no lubricant was dispersed in the base material of the plug, the average actuation force needed was 2.83 pounds. The sample size was 10 and the standard deviation was 0.16. Where the lubricant was dispersed in the base material

of the plug, the average actuation force needed was 2.39 pounds. The sample size was 10 and the standard deviation was 0.29. This data shows that the average reduction in the actuation force was 15.5%. This indicates that the lubricant migrated to the surface of the plug to provide a lubricious surface between the moving parts.

Thus it is seen that a material is provided that exhibits an antimicrobial effect at its surface and that has a lubricious surface and that is especially adapted for use in producing medical devices, whose antimicrobial and lubricious surface characteristics are continually replenished even if the surface of the material is wiped or otherwise used in the normal course of medical procedures.

We claim:

1. A medical article, comprising:
a base material;
a carrier incompatible with the base material blended into the base material; and
an antimicrobial agent encapsulated in the carrier.

2. The medical article of claim 1 further comprising a lubricating agent encapsulated in the carrier.

3. The medical article of claim 2 wherein the carrier and the lubricating agent are the same material.

4. The medical article of claim 3 wherein the base material is a silicone elastomer, the carrier and lubricating agent are a siloxane oil and the antimicrobial agent is chlorhexidine.

5. The medical article of claim 4 wherein the carrier, the lubricating agent and the antimicrobial agent form a carrier solution in which the antimicrobial agent comprises between about 0.5 % by weight and about 10 % by weight of the carrier solution and the carrier solution comprises between about 1 % by weight and about 10 % by weight of the base material.

6. A medical article, comprising:
a base material; and
an antimicrobial agent incompatible with the base material blended into the base material.

7. The medical article of claim 6 wherein the base material is a silicone elastomer and the antimicrobial agent is chlorhexidine.

8. The medical article of claim 7 wherein the antimicrobial comprises between about 0.1 % by weight and about 10 % by weight of the base material.

9. A medical article, comprising:
a base material; and
a lubricating agent incompatible with the base material blended into the base material.

10. The medical article of claim 9 wherein the base material is a silicone elastomer and the lubricating agent is a siloxane oil.

11. The medical article of claim 10 wherein the lubricating agent comprises between about 1 % by weight and about 10 % by weight of the base material.

FIG-1

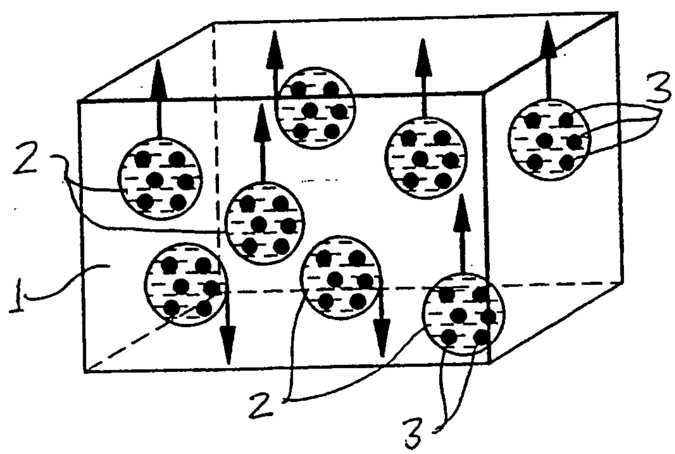
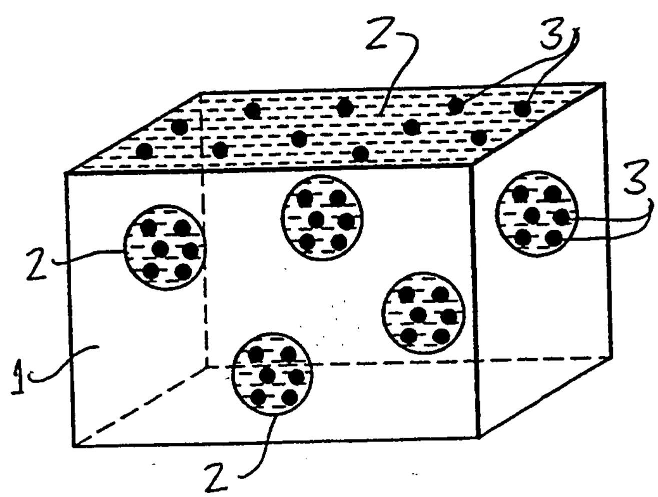


FIG-2



INTERNATIONAL SEARCH REPORT

Intern. ıal Application No
PCT/US 98/27202

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61L29/00 A61L31/00 A61L27/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61L

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 290 271 A (JERNBERG GARY R) 1 March 1994 see column 3, line 23 - column 3, line 60 see column 4, line 17 - column 4, line 26 see column 5, line 56 - column 6, line 24 see figures 1,2,4	1-3,6,9
Y		4,5
X,P	EP 0 882 461 A (UNITIKA LTD) 9 December 1998 see abstract; claim 1	1-3
X	EP 0 379 271 A (BECTON DICKINSON CO) 25 July 1990 see page 2, line 54 - page 3, line 24; claim 6	6-9

-/--

[X] Further documents are listed in the continuation of box C.

[X] Patent family members are listed in annex.

° Special categories of cited documents :

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

Date of the actual completion of the international search	Date of mailing of the international search report
30 March 1999	09/04/1999

Name and mailing address of the ISA	Authorized officer
European Patent Office, P.B. 5818 Patentlaan 2 NL - 2280 HV Rijswijk Tel. (+31-70) 340-2040, Tx. 31 651 epo nl, Fax: (+31-70) 340-3016	Bauer, H

3

INTERNATIONAL SEARCH REPORT

International Application No
PCT/US 98/27202

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication,where appropriate, of the relevant passages	Relevant to claim No.
X	US 5 451 424 A (SOLOMON DONALD D ET AL) 19 September 1995 see column 7, line 28 - column 7, line 37; figure 7	6,8
Y	EP 0 328 421 A (UNIV COLUMBIA) 16 August 1989 see page 2, line 35 - page 3, line 13 see page 8, line 24 - page 9, line 57	4,5

INTERNATIONAL SEARCH REPORT

Information on patent family members

Intern. ,al Application No
PCT/US 98/27202

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5290271 A	01-03-1994	AU 7909691 A	10-12-1991
		CA 2082398 A	15-11-1991
		EP 0528971 A	03-03-1993
		WO 9117744 A	28-11-1991
EP 0882461 A	09-12-1998	JP 10328293 A	15-12-1998
EP 0379271 A	25-07-1990	US 4925668 A	15-05-1990
		AT 96333 T	15-11-1993
		CA 2004367 A,C	18-07-1990
		DE 69004106 D	02-12-1993
		DE 69004106 T	21-04-1994
		ES 2062316 T	16-12-1994
		JP 1839947 C	25-04-1994
		JP 2234764 A	17-09-1990
US 5451424 A	19-09-1995	US 5165952 A	24-11-1992
		US 5013306 A	07-05-1991
		US 5707366 A	13-01-1992
		AT 103497 T	15-04-1994
		CA 2004366 A,C	18-07-1990
		DE 69007631 D	05-05-1994
		DE 69007631 T	25-08-1994
		EP 0379269 A	25-07-1990
		ES 2054229 T	01-08-1994
		IE 64997 B	04-10-1995
		JP 1993226 C	22-11-1995
		JP 2234767 A	17-09-1990
		JP 5023790 B	05-04-1993
		US 4999210 A	12-03-1991
EP 0328421 A	16-08-1989	US 5019096 A	28-05-1991
		AT 88096 T	15-04-1993
		AU 2989589 A	17-08-1989
		AU 636767 B	06-05-1993
		AU 7922991 A	03-10-1991
		JP 2017071 A	22-01-1990
		JP 7090039 B	04-10-1991
		US 5133090 A	28-07-1992
		US 5616338 A	01-04-1997